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CLINICAL ARTICLE

Obstetrics

Clinical features of pregnant women in Iran who died due to COVID-19

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Abstract

Background: To evaluate the clinical presentation of pregnant women in Iran who died due to COVID-19.

Methods: Data were evaluated of pregnant women who died following a laboratory diagnosis of COVID-19. The data were obtained from electronic medical records. Additionally, a questionnaire was completed for each patient, including demographic, clinical, laboratorial, imaging, and treatment data. In case of missing information, a member of the research team contacted the first-degree relatives via phone.

Results: Of 32 pregnant women who tested positive for COVID-19, 15 were enrolled into the study (mean age 30.0 ± 5.0 years). The mean time from first symptoms to death was 12 ± 7.0 days. Pre-existing comorbidities were seen in six patients. The main presentations at admission were fatigue and coughing, but most of the women had a fever below 38 °C. Increased white blood cell count and neutrophils were noticeable. A significant drop of saturation of O_2 with ground glass and consolidation seen in both lungs were prominent. The most common complications were acute respiratory distress syndrome followed by respiratory failure.

Conclusion: Computed tomography findings, O_2 pressure, and regular blood assessment may be considered suitable indicators for the surveillance of patients.

KEYWORDS
COVID-19, Middle East, Mortality, Pregnancy, Presentation

1 | INTRODUCTION

COVID-19 was introduced in December 2019 as a new member of the beta coronavirus family. The virus very quickly became an endemic infection. Hence, its transmission is not a simple issue and the potential modes of transmission need to be considered. Moreover, despite the virus affecting mainly the respiratory system, other vital organs can also be seriously affected.[1,2] Therefore, a broad spectrum of presentation in this situation can be assumed. The mortality rate of COVID-19 is reported to be in the range of 2%–16%, depending on age. Furthermore, the rate of mortality may increase two- to ten-fold among patients admitted to the intensive care unit (ICU) with pre-existing morbidities such as cardiovascular disease and diabetes.[1,3] Li et al.[3] reported that the mortality rate of patients with hypertension, cerebrovascular diseases, and diabetes was two- to three-fold higher in patients admitted to the ICU, respectively. The main risk factors of mortality are older age, shortness of breath or dyspnea, low level of hemoglobin, and underlying comorbidities. Several clinical outcomes such as respiratory failure, acute respiratory distress syndrome (ARDS), septic shock, coagulopathy, acute cardiac injury, and acute kidney injury are significantly higher in non-survivor patients. However, pregnant women as a particular group may be different.[4,5]

In a normal pregnancy, it has been shown that according to physiological changes, a mother's susceptibility to microorganisms (bacteria and viruses) and their products increases.[6] It has been proven that pregnant women are at risk for H1N1 as well as severe acute respiratory syndrome (SARS), Middle East Respiratory Syndrome (MERS), and Ebola infection.[7] Nevertheless, during the COVID-19 pandemic, the fatality rate of pregnant women is not well-known and the effect of this novel virus on the maternal state is unclear. It is assumed that pregnant women are no more likely to get the disease than the general population.[8-10] Previous studies revealed that the virus might not lead to an increased fatality rate during pregnancy.[8,11] In a Swedish report, the risk of being admitted to the ICU was higher in infected pregnant and postpartum women than non-pregnant women of similar ages.[12] Furthermore, in a study of 116 pregnant women in China,[13] the authors concluded that COVID-19 had no effect on pregnancy outcomes. However, there are not many studies regarding non-survivor pregnant patients. The aim of the present study was to illustrate the characteristics of pregnant patients who died in order to identify early critically ill patients with COVID-19 and reduce their mortality.

2 | METHODS

2.1 | Patients

In the present retrospective study, out of 32 pregnant women with COVID-19, the medical files were reviewed for 15 non-survivors who were hospitalized between March 2020 and June 2020 and who died in hospital. The patients were admitted to Firoozgar General Hospital, Iran; a tertiary hospital which has been assigned as one of the referral hospitals for patients with COVID-19. COVID-19 was confirmed in the laboratory according to WHO guidelines (the detection of virus RNA was considered a confirmed positive result).

2.2 | Collection of data

A questionnaire was completed, including demographic, clinical presentation, laboratory, and imaging data. All data were obtained from the electronic files of each patient. In case of any missing data, a member of the team contacted the first-degree relatives of the patient.

2.3 | Laboratory data

All laboratory tests were carried out by the team according to WHO guidelines.[14]

A venous blood sample was obtained from each patient on the first day of admission. Laboratory items were analyzed using diagnostic kits (Pars Azmoon Co., Iran) and Auto-Analyzer BS200 (Mindray, Nanshan, Shenzhen, China).

For the extraction of virus RNA, a nasopharyngeal swab technique was used. Then, a one-step real-time polymerase chain reaction was performed by a referral diagnostic laboratory. In addition, all patients underwent a standard chest computed tomography (CT) scan. The protocol was approved by the Ethics Committee of Firoozgar Hospital.

2.4 | Statistical analysis

The mean ± SD is presented for normal and non-normal continuous variables, respectively. Normal distribution was checked using the Shapiro–Wilk test. Categorical variables were expressed as number (percentage). All statistical analyses were carried out using SPSS version 20.0 (IBM Corp., Armonk, NY, USA).

3 | RESULTS

Overall, 15 pregnant patients who died due to COVID-19 were enrolled. The deaths occurred in the same period of hospitalization. The mean age of the women was 30.0 ± 5.0 years, the mean time of hospitalization was 5.0 ± 3.0 days, and the mean time from first symptoms to death was 12 ± 7.0 days.

Pre-existing comorbidities were seen in six patients: three patients had diabetes mellitus, of whom one had gestational diabetes (Table 1). Interestingly, the majority of patients had a fever below 38°C. As illustrated in Table 2, the main presentations at admission were fatigue, coughing, and myalgia in 11, 10, and five patients,

TABLE 1 Basic characteristics of non-survivor pregnant patients[a]

Variable	Total (n = 15)
Length of stay in hospital (days)	5.0 ± 3.0
Time from first symptoms to admission (days)	6.00 ± 5.07
Time from first symptoms to death (days)	12 ± 7.0
Age (years)	30.0 ± 5.0
Smokers	1 (6.6)
Opium	2 (13.2)
Comorbidities[b]	6 (39.6)
Hypertension	2 (13.2)
Cardiovascular disease	1 (6.6)
Lung disease	0 (0)
Diabetes	3 (19.8)
Renal disease	0 (0)
Liver disease	0 (0)
Neurologic disease	0 (0)
Cancer	0 (0)
Uses of immunosuppressive drugs	0 (0)

[a]Values are given as number (percentage) or mean ± SD.
[b]Comorbidities: Diabetes mellitus or gestational diabetes, cardiovascular disease, and hypertension.

TABLE 2 Clinical findings of non-survivor pregnant patients[a]

Variables	Total (n = 15)
Body temperature (°C)	
<37.5	0 (0)
37.5–38	14 (92.4)
>38.1	1 (6.6)
Sore throat	3 (19.8)
Headache	4 (26.4)
Chest pain	4 (26.4)
Coughing	10 (66)
Production of sputum	1 (6.6)
Fatigue	11 (72.6)
Myalgia/arthralgia	5 (33)
Chills	2 (13.2)
Sweating	2 (13.2)
Shortness of breath	3 (19.8)
Dizziness	2 (13.2)
Nausea and vomiting	4 (26.4)
Abdominal pain	2 (13.2)
Diarrhea	1 (6.6)
Respiratory rate (≥24 breaths per min)	8 (52.8)
Pulse rate (≥120 bpm)	3 (19.8)
CURB score	
2 vs 0–1	2 (13.2)
≥3 vs 0–1	3 (19.8)

[a]Values are given as number (percentage).

respectively. A respiratory rate of more than 24 breaths per minute was also seen in eight patients. The laboratory results at the time of admission are shown in Table 3. It can be seen that increased white blood cell count (WBC) was common among these women. Hence, a WBC more than 10 × 10^9/L was seen in 9 (70%) patients. Although neutrophilia was prominent, lymphopenia was not a common finding and was seen in only four patients. Furthermore, there was no decrease in the levels of hemoglobin or platelets in these patients. Liver function tests, including ALT, AST, and alkaline phosphates, were in the normal ranges in the majority of the pregnant women.

The main finding in the assessment of atrial blood gas was a significant drop in the saturation of O_2. In addition, during an evaluation by CT scan, almost all patients had a ground-glass view in both lungs, and in 11 patients, consolidation was seen in both sides (Table 4). Furthermore, the most common complications were ARDS and respiratory failure in seven and four patients, respectively (Table 5).

4 | DISCUSSION

The present study is a large study regarding non-survivor pregnant patients with COVID-19 in Iran. In the present case series, it was observed that the primary manifestation was a sore throat followed

TABLE 3 The laboratory findings of non-survivor pregnant patients[a]

Variables (normal range)	Total (n = 15)
White blood cell count (4–9.5 × 10^9/L)	12.14 ± 4.7
<4.0	2 (13.3)
4–10	4 (26.6)
>10.0	9 (60)
Neutrophil (1.8–7.4 × 10^9/L)	7.90 ± 1.0
<7000	4 (26.6)
≥7000	11 (73.4)
Lymphocyte (1.0–4.4 × 10^9/L)	1.47 ± 0.8
<1000	4 (26.6)
≥1000	11 (73.4)
Platelets (150–400 × 10^9/L)	171.50 ± 10
>150 000	10 (66.7)
100 000–150 000	1 (6.6)
<100 000	4 (26.6)
Hemoglobin (12–16 g/dL)	11.50 ± 1.8
<10	3 (20)
≥10	12 (80)
Sodium (135–148 mmol/L)	136.12 ± 4.1
<135	5 (33.3)
≥135	10 (66.7)
Potassium (3.5–5.3 mmol/L)	3.8 ± 0.65
<4	12 (80)
≥4	3 (20)
Blood urea nitrogen (7–20 mg/dL)	35.4 ± 6.5
<20	11 (73.4)
≥20	4 (26.6)
Creatinine (0.6–1.4 mg/dL)	0.9 ± 0.2
<1.3	14 (93.4)
≥1.3	1 (6.6)
Total bilirubin (0.1–1.1 mg/dL)	1.10 ± 0.7
<1.7	9 (60)
≥1.7	3 (20)
No. checked	3 (20)
Direct bilirubin (<0.4 mg/dL)	1.0 ± 1.1
<0.5	7 (46.7)
≥0.5	5 (33.3)
No. checked	3 (20)
Alanine transferase (15–40 IU/L)	30.0 ± 20.0
<40	11 (73.4)
≥40	3 (20)
No. checked	1 (6.6)
Aspartate amino transferase (15–40 IU/L)	27.0 ± 20.0
<40	11 (73.4)
≥40	3 (20)
No. checked	1 (6.6)

(Continues)

TABLE 3 (Continued)

Variables (normal range)	Total (n = 15)
Alkaline phosphatase (98–279 U/L)	244.0 ± 130
<280	9 (60.1)
≥280	4 (26.6)
No. checked	2 (13.3)
SPO_2 (>93%)	78.34 ± 16.46
<90	15 (100)
≥90	0 (0)
pH (7.36–7.44)	7.2 ± 0.1
<7.4	8 (53.4)
≥7.4	3 (20)
No. checked	4 (26.6)
CO_2 (36–44 mm Hg)	36.0 ± 2.0
<40	5 (33.3)
≥40	6 (40.1)
No. checked	4 (26.6)
HCO_3 (21–27 nmol/L)	22.80 ± 5.0
<24	6 (40.1)
≥24	5 (33.3)
No. checked	4 (26.6)

[a]Values are given as number (percentage) or mean ± SD.

TABLE 4 Computed tomography findings among non-survivor pregnant patients[a]

Variables	Total (n = 15)
Patchy consolidation on both sides	11 (73.4)
Ground glass	
One side	3 (20)
Both sides	11 (73.4)
Patchy infiltration	
One side	2 (13.2)
Both sides	13 (86.8)

[a]Values are given as number (percentage).

TABLE 5 The complications of COVID-19 infection among non-survival pregnant patients[a]

Variables	Total (n = 15)
Sepsis	1 (6.6)
Respiratory failure	4 (26.6)
ARDS	7 (46)
Septic shock	0 (0)
Coagulopathy	2 (13)
Acute kidney injury	1 (6.6)
Acute cardiac injury	2 (13)
Acidosis	2 (13)

Abbreviation: ARDS, acute respiratory distress syndrome.
[a]Values are given as number (percentage).

by chest pain. High-grade fever was not common. Interestingly, high levels of WBC and neutrophil count, as well as the presence of consolidation on CT evaluation, were ordinary.

According to the results of the present study, the patients were referred to the study center during the last days of their pregnancy for delivery. Hence, they were probably infected in the last month of their pregnancy. In addition, the main clinical presentations were similar to those of general patients with COVID-19. Moreover, the length of hospitalization before death was not longer than that of the general population. This finding is consistent with previous reports.[5,11,15] On the other hand, while older age can be considered a risk factor for worse outcomes in COVID-19 infection,[16] the patients were young; therefore, the possible effect of age might not be significant. Pre-existing comorbidities are a critical issue that need more consideration. Seven patients in the study group had pre-existing comorbidities. Gestational diabetes was seen in one patient. In a previous study, pre-existing comorbidities, particularly hypertension and diabetes, were associated with worse outcomes.

The issue that may need more consideration despite recent epidemiologic studies is the transmission of the virus. As the patients explained, almost all of them had no contact with other patients with COVID-19 during the previous few weeks before developing symptoms of COVID-19. This may be related to the state of emergency at the time of admission, where history taking was not optimal. On other hand, the unknown viral infection with the potential of spreading is not well understood. Hence, its diagnosis and prevention become more difficult. Moreover, the nosocomial transmission of the disease may occur mainly during the incubation period and by close contact with patients with minimal symptoms.[1,17]

It is also not clear whether pregnant women are more prone to contracting COVID-19 compared to the general population, although previous studies have stated that pregnant women are prone to infection due to their "immunosuppressed" state.[18,19] The risk of developing severe symptoms of COVID-19 during pregnancy is not clear[20]; it seems that symptoms tend to be less severe than those of a typical influenza infection.[21]

In the present study, the main complication was respiratory complications presenting as ARDS and respiratory failure. Furthermore, the duration between the first symptoms and death was about 12 days, and they were usually admitted to hospital after 1 week, showing the aggressive and violent nature of the virus in these patients. The results consist of previous reports of ultrasound findings.[22] In fact, COVID-19 can cause multiorgan damage. In previous reports, cardiovascular damage is considered at the top of the list of organ damage in patients with COVID-19.[2,23] However, respiratory side effects were common in the present series, consistent with previous studies including pregnant patients.[24] Furthermore, cardiac and kidney complications must be observed. The patients in the present study were not evaluated regularly for cardiac events. Therefore, cardiac events during hospitalization cannot be confirmed. In fact, the heart may be the target of pulmonary viral infection, either directly or indirectly. The mechanism of organ damage by COVID-19 has not been well understood; It may be related to inflammation pathways and cytokine storms.[2,4]

Regarding prognostic laboratory parameters, in the present study, the other factor that may be associated with worsening of patient outcomes was neutrophilia (>7.7 × 10^9/L). Furthermore, a decrease in levels of lymphocytes and hemoglobin among patients was not observed. Neutrophilia may be associated with acute cardiac events and the development of sepsis, which can increase the odds of mortality. Indeed, a decrease in the level of hemoglobin is associated with poor outcomes and mortality in a previous report.[25] Previous studies reported the critical value of the complete blood count differential, including the levels of lymphocytes and neutrophils as well as hemoglobin, with the patient outcomes.[26]

In conclusion, a pregnant patient is probably at the same risk of developing severe COVID-19 as the general population. The time between admission and death is not long and this needs more attention. It seems that low O_2 saturation, along with consolidation in CT scanning and neutrophilia at admission, can predict worse outcomes.

CONFLICTS OF INTEREST

The authors have no conflict of interest.

AUTHOR CONTRIBUTIONS

SAM, PD, SN, MM, and MH were responsible for substantial contributions to the conception or design of the work, and the acquisition, analysis, or interpretation of data; MS was responsible for drafting the work and revising it critically for important intellectual content. SAM was responsible for the final version for publication. MS agreed to be accountable for all aspects of the work, and in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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